IUCLID

Data Set

Existing Chemical	:	ID: 66346-01-8
CAS No.	:	66346-01-8
EINECS Name	:	1-(4-Chlorphenyl)-4,4-dimethyl-3-pentanon
Molecular Formula	:	C13H17OCl
Producer related part		
Company	:	Epona Associates, LLC
Creation date	:	10.01.2008
Substance related part		
Company	:	Epona Associates, LLC
Creation date	:	10.01.2008
Status	:	
Memo	:	
Printing date	:	31.01.2008
Revision date	:	
Date of last update	:	31.01.2008
Number of pages	:	2
Chapter (profile)	:	Chapter: 1, 2, 3, 4, 5, 6, 7, 8, 10
Reliability (profile)	:	Reliability: without reliability, 1, 2, 3, 4
Flags (profile)	:	Flags: without flag, confidential, non confidential, WGK (DE), TA-Luft (DE), Material Safety Dataset, Risk Assessment, Directive 67/548/EEC, SIDS

1.0.1 APPLICANT AND COMPANY INFORMATION

Type	:	manufacturer
Name	:	Bayer Corporation
Contact person	:	
Date	:	
Street	:	100 Bayer Road, Building #14
Town	:	PA 15205-9741 Pittsburgh
Country	:	United States
Phone	:	
Telefax	:	
Telex	:	
Cedex	:	
Email	:	
Homepage	:	

Source : Bayer Corporation Pittsburgh
17.11.2003

1.0.2 LOCATION OF PRODUCTION SITE, IMPORTER OR FORMULATOR

1.0.3 IDENTITY OF RECIPIENTS

1.0.4 DETAILS ON CATEGORY/TEMPLATE

1.1.0 SUBSTANCE IDENTIFICATION

IUPAC Name	:	1-(4-chlorophenyl)-4,4-dimethyl pentanone
Smiles Code	:	O=C(C(C)(C)C)CCc1ccc(cc1)CL
Molecular formula	:	C13 H17 Cl O
Molecular weight	:	224.75
Petrol class	:	

Source : Bayer Corporation Pittsburgh
17.11.2003

1.1.1 GENERAL SUBSTANCE INFORMATION

Purity type	:	other: technical material
Substance type	:	organic
Physical status	:	liquid
Purity	:	ca. 99.8 % v/v
Colour	:	yellow
Odour	:	

Source : Bayer Corporation Pittsburgh
17.12.2003

1.1.2 SPECTRA

1.2 SYNONYMS AND TRADENAMES

1-(p-Chlorophenyl)-4,4-dimethylpentan-3-one

Source : Bayer Corporation Pittsburgh
19.11.2003

HWG Alkylketone

Source : Bayer Corporation Pittsburgh
19.11.2003

1.3 IMPURITIES

1.4 ADDITIVES

1.5 TOTAL QUANTITY

1.6.1 LABELLING

1.6.2 CLASSIFICATION

1.6.3 PACKAGING

1.7 USE PATTERN

1.7.1 DETAILED USE PATTERN

1.7.2 METHODS OF MANUFACTURE

1.8 REGULATORY MEASURES

1.8.1 OCCUPATIONAL EXPOSURE LIMIT VALUES

1.8.2 ACCEPTABLE RESIDUES LEVELS

1.8.3 WATER POLLUTION

1.8.4 MAJOR ACCIDENT HAZARDS

1.8.5 AIR POLLUTION

1.8.6 LISTINGS E.G. CHEMICAL INVENTORIES

1.9.1 DEGRADATION/TRANSFORMATION PRODUCTS

1.9.2 COMPONENTS

1.10 SOURCE OF EXPOSURE

1.11 ADDITIONAL REMARKS

1.12 LAST LITERATURE SEARCH

1.13 REVIEWS

2.1 MELTING POINT

Value	:	18 °C
Sublimation	:	
Method	:	other
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	pour point: ca. 18 degrees C solidifying range: 10 - 16 degrees C
Source	:	Bayer Corporation Pittsburgh
Flag	:	Critical study for SIDS endpoint

11.01.2008 (20)

2.2 BOILING POINT

Value	:	270 °C at
Decomposition	:	
Method	:	other
Year	:	
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	The value of 270 ºC provided on the Bayer MSDS is similar to the value of approximately 290 ºC estimated using EPIWIN version 3.12
Source	:	Bayer Corporation Pittsburgh
Flag	:	Critical study for SIDS endpoint

11.01.2008 (8)

2.3 DENSITY

Type	:	density
Value	:	ca. 1.049 g/cm³ at 20 °C
Method	:	other: DIN 51757
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Bayer Corporation Pittsburgh

11.01.2008 (20)

2.3.1 GRANULOMETRY

2.4 VAPOUR PRESSURE

Value	:	.00066 hPa at 20 °C
Decomposition	:	
Method	:	
Year	:	1992
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4

Source : Bayer Corporation Pittsburgh
Flag : Critical study for SIDS endpoint
11.01.2008 (2)

Value : .017 hPa at 50 °C
Decomposition :
Method :
Year : 1992
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer Corporation Pittsburgh
11.01.2008 (2)

Value : .027 hPa at 55 °C
Decomposition :
Method :
Year : 1992
GLP : no data
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer Corporation Pittsburgh
11.01.2008 (2)

2.5 PARTITION COEFFICIENT

Partition coefficient : octanol-water
Log pow : 3.97 at 25 °C
pH value :
Method : other (calculated): KOWWIN Program (v1.67)
Year : 2000
GLP : no
Test substance : other TS: molecular structure of 3-Pentanone, 1-(4-chlorophenyl)-4,4-dimethyl- (CAS# 66346-01-8)

Result : Log Kow(version 1.67 estimate): 3.97
SMILES : O=C(C(C)(C)C)CCc1ccc(cc1)CL
CHEM : 3-Pentanone, 1-(4-chlorophenyl)-4,4-dimethyl-
MOL FOR: C13 H17 CL1 O1
MOL WT : 224.73

TYPE	NUM	LOGKOW FRAGMENT DESCRIPTION	COEFF	VALUE
Frag	3	-CH3 [aliphatic carbon]	0.5473	1.6419
Frag	2	-CH2- [aliphatic carbon]	0.4911	0.9822
Frag	6	Aromatic Carbon	0.2940	1.7640
Frag	1	-CL [chlorine, aromatic attach]	0.6445	0.6445
Frag	1	-C(=O)- [carbonyl, aliphatic attach]	-1.5586	-1.5586
Frag	1	-tert Carbon [3 or more carbon attach]	0.2676	0.2676
Const		Equation Constant		0.2290

Log Kow = 3.9706
Source : Bayer Corporation Pittsburgh
Reliability : (2) valid with restrictions
modeled data
Flag : Critical study for SIDS endpoint
11.01.2008 (13)

2.6.1 SOLUBILITY IN DIFFERENT MEDIA

Solubility in	:	Water
Value	:	20.7 mg/l at 20 °C
pH value	:	
concentration	:	at °C
Temperature effects	:	
Examine different pol.	:	
pKa	:	at 25 °C
Description	:	
Stable	:	
Deg. product	:	
Method	:	other: Kolbenmethode
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Bayer Corporation Pittsburgh
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

11.01.2008 (4)

2.6.2 SURFACE TENSION

2.7 FLASH POINT

Value	:	145 °C
Type	:	
Method	:	other: DIN 51758
Year	:	1988
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Source	:	Bayer Corporation Pittsburgh

11.01.2008 (20)

2.8 AUTO FLAMMABILITY

2.9 FLAMMABILITY

2.10 EXPLOSIVE PROPERTIES

2.11 OXIDIZING PROPERTIES

2.12 DISSOCIATION CONSTANT

2.13 VISCOSITY

2.14 ADDITIONAL REMARKS

3.1.1 PHOTODEGRADATION

Type	:	air
Light source	:	
Light spectrum	:	nm
Relative intensity	:	based on intensity of sunlight
INDIRECT PHOTOLYSIS		
Sensitizer	:	OH
Conc. of sensitizer	:	1500000 molecule/cm³
Rate constant	:	.0000000000077665 cm³/(molecule*sec)
Degradation	:	50 % after 16.5 hour(s)
Deg. product	:	
Method	:	other (calculated): AOP Program (v1.91)
Year	:	2000
GLP	:	no
Test substance	:	other TS: molecular structure of 3-Pentanone, 1-(4-chlorophenyl)-4,4-dimethyl- (CAS# 66346-01-8)
Source	:	Bayer Corporation Pittsburgh
Reliability	:	(2) valid with restrictions modeled data
Flag	:	Critical study for SIDS endpoint

11.01.2008 (13)

3.1.2 STABILITY IN WATER

Type	:	abiotic
t1/2 pH4	:	at °C
t1/2 pH7	:	at °C
t1/2 pH9	:	at °C
Deg. product	:	
Method	:	
Year	:	
GLP	:	no
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	Based on similar compounds and experience, this compound is expected to be extremely stable in water (>1 year at pH 5 - 9).
Source	:	Bayer Corporation Pittsburgh

11.01.2008 (9)

3.1.3 STABILITY IN SOIL

3.2.1 MONITORING DATA

3.2.2 FIELD STUDIES

3.3.1 TRANSPORT BETWEEN ENVIRONMENTAL COMPARTMENTS

Type	:	fugacity model level III
Media	:	other: air - water - soil - sediment

Air	:	% (Fugacity Model Level I)
Water	:	% (Fugacity Model Level I)
Soil	:	% (Fugacity Model Level I)
Biota	:	% (Fugacity Model Level II/III)
Soil	:	% (Fugacity Model Level II/III)
Method	:	other: Level III Fugacity Model
Year	:	2000
Remark	:	Modeling was performed using equal releases (300 kg/hr) and equal distribution to all compartments
Result	:	Chem Name: 3-Pentanone,1-(4-chlorophenyl)-4,4-dimethyl- Molecular Wt: 224.73 Henry's LC : 9.21e-006 atm-m3/mole (Henrywin program) Vapor Press : 0.00049 mm Hg (user-entered) Log Kow : 3.97 (Kowwin program) Soil Koc : 3.83e+003 (calc by model)

	Mass Amount (%)	Half-Life (hr)	Emissions (kg/hr)
Air	1.16	33	300
Water	22.3	1.44e+003	300
Soil	72.5	1.44e+003	300
Sediment	3.99	5.76e+003	0

	Fugacity (atm)	Reaction (kg/hr)	Advection (kg/hr)	Reaction (%)	Advection (%)
Air	1.08e-011	210	99.9	23.3	11.1
Water	3.91e-011	92.5	192	10.3	21.4
Soil	1.55e-011	301	0	33.4	0
Sediment	3.8e-011	4.14	0.688	0.46	0.0765

Persistence Time: 958 hr
Reaction Time: 1.42e+003 hr
Advection Time: 2.94e+003 hr
Percent Reacted: 67.5
Percent Advected: 32.5

Source	:	Bayer Corporation Pittsburgh
Reliability	:	(2) valid with restrictions modeled data
Flag	:	Critical study for SIDS endpoint

11.01.2008 (13)

3.3.2 DISTRIBUTION

3.4 MODE OF DEGRADATION IN ACTUAL USE

3.5 BIODEGRADATION

Contact time	:	
Degradation	:	(±) % after
Result	:	other: NOT Readily Degradable
Deg. product	:	
Method	:	other: BIOWIN (v4.01)
Year	:	
GLP	:	no
Test substance	:	other TS: molecular structure of 3-Pentanone, 1-(4-chlorophenyl)-4,4-dimethyl- (CAS# 66346-01-8)

Result	:	BIOWIN (v4.01) Program Results: ========== SMILES : O=C(C(C)(C)C)CCc1ccc(cc1)CL CHEM : 3-Pentanone, 1-(4-chlorophenyl)-4,4-dimethyl- MOL FOR: C13 H17 CL1 O1 MOL WT : 224.73 ---------- BIOWIN v4.01 Results ---------- Linear Model Prediction : Does Not Biodegrade Fast Non-Linear Model Prediction: Does Not Biodegrade Fast Ultimate Biodegradation Timeframe: Months Primary Biodegradation Timeframe: Weeks ********** MITI Linear Model Prediction: p=0.2629 MITI Non-Linear Model Prediction: p=0.1086 A Probability Less Than 0.5 indicates --> NOT Readily Degradable
Source	:	Bayer Corporation Pittsburgh
Reliability	:	(2) valid with restrictions modeled data
Flag	:	Critical study for SIDS endpoint

11.01.2008 (13)

Contact time	:	
Degradation	:	(±) % after
Result	:	under test conditions no biodegradation observed
Deg. product	:	
Method	:	other: EEC official gazette L 383A, Part C (c.4-D) "Manometric Respirometry" (29.12.92)
Year	:	1995
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Source	:	Bayer Corporation Pittsburgh
Test substance	:	Purity = 99.1%
Reliability	:	(1) valid without restriction
Flag	:	Critical study for SIDS endpoint

11.01.2008 (7)

3.6 BOD5, COD OR BOD5/COD RATIO

3.7 BIOACCUMULATION

Species	:	Brachydanio rerio (Fish, fresh water)
Exposure period	:	at °C
Concentration	:	
Elimination	:	
Method	:	OECD Guide-line 305 E "Bioaccumulation: Flow-through Fish Test"
Year	:	1995
GLP	:	yes
Test substance	:	other TS: 99,1 %

Source	:	Bayer Corporation Pittsburgh

31.01.2008 (6)

3.8 ADDITIONAL REMARKS

4.1 ACUTE/PROLONGED TOXICITY TO FISH

Type	:	static
Species	:	Leuciscus idus (Fish, fresh water)
Exposure period	:	96 hour(s)
Unit	:	mg/l
NOEC	:	3.16
LC50	:	ca. 4.9
Limit test	:	
Analytical monitoring	:	yes
Method	:	OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method :

Reconstituted water, containing the ion concentrations listed below, was continuously produced by addition of saline solutions to demineralized water.
Ca++ 0.384 mMol/l; Mg++ 0.096 mMol/l; Na+ 0.148 mMol/l;
K+ 0.015 mMol/l; HCCT 0.148 mMol/l; Cf3 0.783 mMol/l;
S04~ 0.096 mMol/l.
The water was continuously ventilated in a 2000 I supply tank.
pH: 7.1-7.3; Oxygen: 7.1 - 9.0 mg/l; Temperature: 22°C;
Ventilation: approx. 200 ml air/min prior to and during the test; Total hardness: 48 mg CaCos/l (2.7° dH) nominal, 3.2° dH measured;
Illumination: 16 hours light (0500 - 2100 h MEZ)/ 8 hours dark.
The nominal concentrations tested were 1.00, 1.80, 3.16, 5.62 and 10.00 mg a.i./l as well as a solvent control (0.1 ml acetone/1). All concentrations given refer to mg a.i./l and are corrected for the purity of the technical active ingredient.
A control without solvent was not tested, because according to our experience acetone in the concentration used does not affect the fish in these kinds of tests.

Remark :

The LC50-values given in this report refer to measured values, because analytical control of the concentrations showed that with the exception of the highest concentration (10.0 mg active ingredient (a.i.)/l) the mean measured values were greater than 80 % of the nominal values in all aquaria.
All other data (NOEC, LLC) refer to nominal concentrations, because in these concentrations over 80% of the respective nominal values were found by analysis.

Result :

The 96-hour LC50 of the technical active ingredient (a.i.) was determined to be 4.9 mg a.i./l with a 95 % confidence from 4.0 to 6.6 mg a.i./l. (LITCHFIELD and WILCOXON).
The lowest lethal concentration was 5.62 mg a.i./l, and the producing no highest concentration toxic effects (NOEC) was 3.16 mg a.i./l.

Mortality and Symptoms of Intoxication
(dead/symptoms/tested)(description of symptoms)

Nominal conc. (mg a.i./l)	48 hours	72 hours	96 hours
Solvent control	0/0/10	0/0/10	0/0/10
1.00	0/0/10	0/0/10	0/0/10
1.80	0/0/10	0/0/10	0/0/10
3.16	0/10/10 SN	0/10/10 SN	0/0/10
5.62	1/10/10 SR	2/10/10 SR	3/10/10
10.00	--	--	--

LC50 (mg a.i./l) 5.47 5.18 4.92
95%-confidence int. -- 4.18-7.04 3.99-6.57
Abbreviations used to describe the Symptoms of Intoxication
SN: Swimming behaviour slightly irregular (light symptom)
SR: Lying on side/back

Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
11.01.2008 (14)

Type : static
Species : Salmo gairdneri (Fish, estuary, fresh water)
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : .89
LC50 : ca. 3.74
Limit test :
Analytical monitoring : yes
Method : OECD Guide-line 203 "Fish, Acute Toxicity Test"
Year : 1988
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The nominal concentrations tested were 0.50, 0.89, 1.58, 2.81 and 5.00 mg a.i./l as well as a solvent control (0.1 ml acetone/1). All concentrations given refer to mg a.i./l and are corrected for the purity of the technical active ingredient. A control without solvent was not tested, because according to our experience acetone in the concentration used does not affect the fish in these kind of tests.
The analytical results show that the active ingredient was stable over the test duration under the conditions of this study.

Wasser Rekonstituiertes Wasser mit der unten genannten lonen-Zusammensetzung wurde kontinuierlich durch die Zugabe von Salzlbsungen zu demineralisiertem Wasser
hergestellt: Ca 0.384 mMol/l; Mg++ 0.096 mMol/l;Na+ 0.148 mMol/l; K+ 0.015 mMol/l; HC03- 0.148 mMol/l; Cl 0.783 mMol/l; SO/- 0.096 mMol/l.

Das Wasser wurde in einem 2000 1 Vorratsbehalter continuierlich beluftet. pH: 7,2 - 7,4; Sauerstoff: 10,7 - 12,0 mg/l,;
Belueftung: ca. 200 ml Luft/min vor und wahrend des Tests; Gesamtharte: 48 mg CaC03/l (2,7° dH) nominal
3,2° dH gemessen; Beleuchtung: 16 Stunden Licht (0500 - 2100 Uhr MEZ)/ 8 Stunden dunkel.

Remark : The values given in this report refer to nominal values, because analytical control of the concentrations showed that with the exception of the lowest concentration (0.50 mg active ingredient (a.i.)/l) the mean measured values were greater than 80 % of the nominal values in all aquaria.

Result : The 96-hour LC50 of the technical active ingredient was determined to be 3.74 mg a.i./l with a 95 % confidence interval from 2.81 to 5.00 mg a.i./l. The confidence interval is derived from two adjacent concentrations spaced by a factor of 1.78, in which 0 and 100 % mortality have been observed. The lowest lethal concentration was 5.00 mg a.i./l, and the no-observedeffect- concentration (NOEC) 0.89 mg a.i./l. In the next higher concentration (1.58 mg a.i./l) only slight changes in the behaviour of the fish was observed.

Mortality and Symptoms of Intoxication
(dead/symptoms/tested)(description of symptoms)

Nominal conc. (mg a.i./l)	48 hours	72 hours	96 hours

Solvent Control 0/0/10 0/0/10 0/0/10
0,50 0/0/10 0/0/10 0/0/10
0,89 0/0/10 0/0/10 0/0/10
1,58 0/0/10 0/10/10 0/10/10
SN SN
2,81 0/10/10 0/10/10 0/10/10
SN, DF SN, DF SN, DF
5,00 10/10/10 -- --
SN, DF
LC50 3,74 3,74 3,74
95 %-Vertrauens 2,81-5,00 2,81-5,00 2,81-5,00
DF : Dark coloration
SN : Swimming behaviour slightly irregular (light symptom)

Source : Bayer Corporation Pittsburgh
Test substance : Purity = 95.4 %
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
11.01.2008 (15)

4.2 ACUTE TOXICITY TO AQUATIC INVERTEBRATES

Type : static
Species : Daphnia magna (Crustacea)
Exposure period : 48 hour(s)
Unit : mg/l
NOEC : .1
EC50 : 3.2
LOEC : 1
Analytical monitoring : no
Method : OECD Guide-line 202
Year : 1988
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Main study
Temperature: 20.5 degree C
pH-value (control beaker): 7.96
(lowest concentration): 7.96
(highest concentration): 7.99
Oxygen saturation (control beaker): 102%
(lowest concentration): 102%
(highest concentration): 101%
The EC50 determination was by Probit-Analysis after the "Maximum-Likelihood" Method using a calculator.

Remark : The numbers quoted are nominal concentrations, since an analytical check of the test concentrations is not
included in the specified Guideline for this 48 hour acute test.

Result : The EC50 for Daphnia maqna after 24 hours was 5.9 mg a.i./litre (95% confidence limits 3.8 - 14.5 mg/litre), after 48 hours 3.2 mg a.i./litre (95% confidence limits not calculable). The 'no-observed-effect-concentration' (NQEC) (48 hours) was 0.1 mg a.i./litre. The lowest-observed-effect-concentration' (LOEC) was 1.0 mg
a.i./litre.

Concentration (mg a.i./litre)	Number living 24 hours	Number living 48 hours	%Immobilised (symptoms) 24 hours	%Immobilised (symptoms) 48 hours
Control	30	30	0	0
10.0	0(2,3)	0	100	100
5.6	20(1,3)	2(1,3)	33	93
3.2	30(1,3)	27(1,3)	0	10

1.8	30(1,3)	24(1,3)	0	20
1.0	29(1,3)	2 (1,3)	3	13

symptoms:
1) Hardly any movements perceivable.
2) Animals cling to the water surface.
3) Animals lie at the bottom.

Source : Bayer Corporation Pittsburgh
Test substance : Purity = 95.4 %
Reliability : (1) valid without restriction
Flag : Critical study for SIDS endpoint
31.01.2008 (16)

4.3 TOXICITY TO AQUATIC PLANTS E.G. ALGAE

Species : other algae: Pseudokirchneriella subcapitata
Endpoint : growth rate
Exposure period : 96 hour(s)
Unit : mg/l
NOEC : 1.2
LOEC : 2.8
EC50 : 3.3
Limit test : no
Analytical monitoring : yes
Method : OECD Guide-line 201 "Algae, Growth Inhibition Test"
Year : 2007
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The green algae Pseudokirchneriella subcapitata were exposed under static (shaken cultures) conditions for 96-hours. Nominal concentrations were control, solvent control, 0.63, 1.25, 2.5, 5.0 and 10 mg a.i./L. Nominal concentrations were control, solvent control, 0.63, 1.25, 2.5, 5.0 and 10 mg a.i./L. The toxicity values were calculated based on the initial measured concentrations
due to degradation of test material in the test system.

Result : Nominal concentrations were control, solvent control, 0.63, 1.25, 2.5, 5.0 and 10 mg a.i./L. The corresponding initial measured recoveries were 0 (control), 0 (solvent control), 0.61, 1.20, 2.8, 4.7, and 11.0 mg/L representing a range of
93 to 113% of the nominal concentrations. The 96-hour measured recoveries ranged from 66 to 87% of the nominal concentrations. No physical abnormalities were observed in the controls or treatment groups during the study.
Conclusions: The 72 and 96-hour growth rates were calculated based on initial measured concentrations. The 72 hour EC50 value for growth rate (ErC50) is 3.1 mg a.i./L with LOEC and NOEC values of 2.8 and 1.2 mg a.i./L, respectively. The 96-hour EC50 value for growth rate is 3.3 mg a.i./L with LOEC and NOEC values of 2.8 and 1.2 mg a.i./L, respectively. The Cumulative Biomass
EbC50 (95% Confidence Intervals): 2.5 mg a.i./L (2.0 to 3.0 mg a.i./L)with NOEC and LOEC values of 2.8 and 1.2 mg a.i./L.

Test substance : 99.2% pure
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
11.01.2008 (10)

4.4 TOXICITY TO MICROORGANISMS E.G. BACTERIA

Type	:	aquatic
Species	:	activated sludge
Exposure period	:	24 hour(s)
Unit	:	mg/l
EC50	:	> 10000
Analytical monitoring	:	no
Method	:	ISO 8192 "Test for inhibition of oxygen consumption by activated sludge"
Year	:	1993
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Remark	:	39.9 % inhibition at 10000 mg/l direct weight
Source	:	Bayer Corporation Pittsburgh

31.01.2008 (3)

4.5.1 CHRONIC TOXICITY TO FISH

4.5.2 CHRONIC TOXICITY TO AQUATIC INVERTEBRATES

4.6.1 TOXICITY TO SEDIMENT DWELLING ORGANISMS

4.6.2 TOXICITY TO TERRESTRIAL PLANTS

4.6.3 TOXICITY TO SOIL DWELLING ORGANISMS

4.6.4 TOX. TO OTHER NON MAMM. TERR. SPECIES

4.7 BIOLOGICAL EFFECTS MONITORING

4.8 BIOTRANSFORMATION AND KINETICS

4.9 ADDITIONAL REMARKS

5.0 TOXICOKINETICS, METABOLISM AND DISTRIBUTION

5.1.1 ACUTE ORAL TOXICITY

Type	:	LD50
Value	:	ca. 4748 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	50
Vehicle	:	other: demineralized water using 2% Cremophor EL
Doses	:	500, 1000, 25000, 4000 (males only), 5000 mg/kg bw
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1988
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method :

Before administration, the test article was formulated in demineralized water using 2% Cremophor EL (v/v).
The test article was administered in a single dose per os by gavage to fasted (approx. 17 hours ± 1 hour) male and female rats (5 animals per dose and sex).
The volume administered was 10 ml/kg body weight. The animals were allowed to feed two hours after treatment.
Appearance and behaviour was recorded several times on the day of treatment, and at least once a day thereafter.
The post-treatment observation period was 14 days.
The animals were sacrificed at the end of the post-treatment observation period using diethyl ether and
subjected to a gross pathology examination, as were any animals which died intercurrently. Where it was possible to calculate the mean (median) lethal dose (LD50) this was done by means of computer (HP 3000) in the manner described by ROSIELLO et al. J. Tox. Environ. Health. 3:797-809 (1977).

Result :

NOEL = 500 mg/kg bw.
LD50 oral (male) : approx. 4748 mg/kg. body weight.

Dose (mg/kg bw)	Results (death/toxic signs/#animals)	Time of death
500	0 /0 /5	-
1000	0 /5 /5	-
2500	0 /5 /5	-
4000	1 /5 /5	3 days
5000	3 /5 /5	1-3 days

LD50 oral (female): >5000 mg/kg. body weight.

Dose (mg/kg bw)	Results (death/toxic signs/#animals)	Time of death
500	0 /0 /5	-
1000	0 /5 /5	-
2500	0 /5 /5	-
5000	2 /5 /5	3 days

1000 mg/kg bw: female rats showed an increase in urine excretion; soft feces, apathy and staggering were
additionally observed in the male rats at this dose.
2500 mg/kg bw onwards: females additionally
exhibited signs of apathy, piloerection and soft feces.
>/=2500 mg/kg bw (male rats) and 5000 mg/kg bw (female rats): respiration difficulties, reduced motility, muscular spasms, prostration or

lying on side, poor or no reflexes and dilated pupils, as well as isolated episodes of spastic gait or staggering, weight reduction and increased motility. Signs were observed shortly after administration, and lasted until day 6 of the post-treatment observation period (except females in the 1000 mg/kg. body weight dose group - here urine excretion increased from day 2 until day 4).

Source : Bayer Corporation Pittsburgh
Test substance : HWG 1608 - Alkylketone; Purity = 99.0 % (analytical findings, APF of 02.05.88)
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
14.01.2008 (1)

Type : LD50
Value : ca. 3145 mg/kg bw
Species : rat
Strain : Wistar
Sex : male
Number of animals : 5
Vehicle : water
Doses : 500, 1000, 2000, 2500, 3550, 4000, 5000 mg/kg bw
Method : OECD Guide-line 401 "Acute Oral Toxicity"
Year : 1981
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : The test compound was emulsified in deionized water using Cremophor EL (2%). A single dose (volume = 10 ml/kg bw) was administered by oral gavage to male and female rats that had been fasted for 16 hours (5 animals /sex/dose). Two hours after administration, feed was again made available to the animals. The animals were observed for 14 days, after which the survivors were sacrificed. All animals were subjected to gross pathological examination.
The median lethal dose (LD50) was calculated by computer (HP 3000) by the method of AP Rosiello, JM Essigmann, and GN Wogan 1977. J. Tox. and Environ. Health. 3:797-809).

Result : male: LD 50 = 2406-4112 mg/kg

Dose (mg/kg bw)	Results (death/toxic signs/#animals)	Time of death
500	0 /0 /5	-
1000	0 /5 /5	-
2000	1 /5 /5	2 days
2500	2 /5 /5	280 hr -3 days
3550	2 /5 /5	1-2 days
4000	3 /5 /5	1-3 days
5000	5 /5 /5	1-2 days

Toxic signs included piloerection, lethargy, reduced activity, hyporeflexia, staggering gait with lateral and sternal recumbency, convulsions, tachypnea, and difficulty breathing, polyuria, and soft feces.
Gross pathology findings of animals that died during the observation period included ulcer-like foci in forestomach; reddened and mucoid content in glandular stomach and intestinal tract; distended, dark red and mottled lungs; lobular patterned liver; dark spleen; pale and mottled kidneys; urinary bladder filled with red urine.
Animals sacrificed at end of observation period had no indications of test compound-related gross organ damage.

Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
14.01.2008 (21)

Type	:	LD50
Value	:	4823 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	female
Number of animals	:	5
Vehicle	:	water
Doses	:	
Method	:	OECD Guide-line 401 "Acute Oral Toxicity"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The test compound was emulsified in deionized water using Cremophor EL (2%). A single dose (volume = 10 ml/kg bw) was administered by oral gavage to male and female rats that had been fasted for 16 hours (5 animals /sex/dose). Two hours afer administration, feed was again made available to the animals. The animals were observed for 14 days, after which the survivors were sacrificed. All animals were subjected to gross pathological examination.
The median lethal dose (LD50) was calculated by computer (HP 3000) by the method of AP Rosiello, JM Essigmann, and GN Wogan 1977. J. Tox. and Environ. Health. 3:797-809).

Result : Female: LD 50 = 3138-7414 mg/kg

Dose (mg/kg bw)	Results (death/toxic signs/#animals)	Time of death
500	0 /0 /5	-
1000	0 /5 /5	-
2500	1 /5 /5	4 days
5000	2 /5 /5	1-3 days
7100	4 /5 /5	1-2 days

Toxic signs included piloerection, lethargy, reduced activity, hyporeflexia, staggering gait with lateral and sternal recumbency, convulsions, tachypnea, and difficulty breathing, polyuria, and soft feces.
Gross pathology findings of animals that died during the obsrvation period included ulcer-like foci in forestomach; reddened and mucoid content in glandular stomach and intestinal tract; distended, dark red and mottled lungs; lobular patterned liver; dark spleen; pale and mottled kidneys; urinary bladder filled with red urine.
Animals sacrificed at end of observation period had no indications of test compound-related gross organ damage.

Source	:	Bayer Corporation Pittsburgh
Reliability	:	(1) valid without restriction Guideline study

14.01.2008 (21)

5.1.2 ACUTE INHALATION TOXICITY

Type	:	LC50
Value	:	> 2938 mg/m³
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: polyethylene glycol E 400 - ethanol mixture (1:1)
Doses	:	412, 1437, 2938 mg/m3 (measured)
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	

GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	Appearance and behaviour were individually assessed several times on the day of exposure. The rats were also assessed during the weekends. The post-treatment observation period lasted 2 weeks. Body weights were recirded before exposure and on day 3 and 7 of the post-treatment observation period. The animals were sacrificed at the end of the post-treatment observation period with sodium hexobarbital [Evipan-Natrium®] (350 mg/kg b.w., i.p. administration) and subjected to a gross pathology examination. All abnormal findings were recorded. Control group: In order to determine exposure-induced effects on body weight gain in acute head-nose only exposed rats using the administration route described, rats are exposed under study conditions once every 3 months to the solvents normally used in inhalation toxicity testing, as follows (1x4 hours head-nose only exposure; 10 males and 10 females per group): air, water/aerosol (nominal 500000 /il/m3 air), and polyethylene glycol E 400-ethanol (1:1) aerosol (nominal 20000 /fl/m3 air) . If it is possible to calculate the mean (median) lethal concentration (LC50) this is done by computer (HP 3000) according to the A.P. Rosiello et al.,1977 (J. Tox. Environ. Health. 3:797-809), with modifications by Pauluhn, J. 1983 (Bayer AG, Report No. 11835). Head/nose only exposure over 4 hours, dynamic exposure conditions, 2 - week post-treatment observation period. The aerosol test atmosphere was generated by nebulizing the test article with a polyethylene glycol E 400 - ethanol mixture (1:1) as a vehicle. During aerosol generation the ethanol present in the vehicle evaporates, thereby promoting the formation of smaller particles. As far as was technically possible, the efficiency of the aerosol generation system was monitored using an aerosol photometer. Sampling was performed continuously in the breathing zone in the immediate vicinity of the rats. 100% of the particles were less than 5 microns in size.
Result	:	NOEL =2938 mg/m3 air. The test article aerosol produced no acute inhalation toxicity in the rat up to and including the max. tested concentration of 2938 mg/m3 air. The exposure was tolerated without clinical signs.
Source	:	Bayer Corporation Pittsburgh
Test substance	:	Purity = 99.0%
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

14.01.2008 (22)

Type	:	LC50
Value	:	> 1370 mg/m³
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	250, 1000, 500, 5000 mg/m3 (nominal); 71.6, 280.9, 739.4, 1369.9 mg/m3 (measured)
Exposure time	:	4 hour(s)
Method	:	OECD Guide-line 403 "Acute Inhalation Toxicity"
Year	:	1981
GLP	:	yes

Test substance	:	as prescribed by 1.1 - 1.4
Method	:	The test compound was dissolved in a mixture of polyethylene glycol E 400 (Lutrol)/ethanol (1:1) and nebulized as an aerosol into a 40 liter inhalation chamber under dynamic conditions. From historical studies, 90% of aerosol exhibits a mass accessible to the alveoli (MMAD about 2 um; 90% less than 5 um). Five animals per sex per concentration were exposed nose-only to the aerosol for a period of 4 hours. Air samples were obtained in the breathing zone of the rats and the concentration determined indirectly by oil red analysis (oil red was mixed at 0.05% with the test compound and determined spectrophotometrically at 525 nm). The animals were observed for 14 days, after which the survivors were sacrificed. All animals were subjected to gross pathological examination. The median lethal concentration (LC50) was calculated by computer (HP 3000) by the method of AP Rosiello, JM Essigmann, and GN Wogan 1977. J. Tox. Environ. Health. 3:797-809).
Result	:	Concentration Results Time of death (mg/m3) (death/toxic signs/#animals) 71.6 0 /0 /10 - 280.9 0 /10/10 - 739.4 0 /10/10 - 1369.9 0 /10/10 - Toxic signs included reduced activity (only on day of exposure), piloerection and unpreened hair coat. Gross pathology findings included lobular pattern of the liver; distended lungs with dark red and gelatinous changed zones.
Source	:	Bayer Corporation Pittsburgh
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

14.01.2008 (21)

Type	:	other
Value	:	> 179 - 214 mg/m³
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	
Exposure time	:	7 hour(s)
Method	:	other
Year	:	1984
GLP	:	no data
Test substance	:	as prescribed by 1.1 - 1.4
Method	:	A constant stream of air was passed via a fritted glass filter of approximately 5 cm diameter through a vessel containing 100 ml of the test compound. The vessel was exchanged every 30 minutes. Five male or female rats were placed in a 10 liter chamber and subjected to whole-body exposure to test substance constituents that were volatile at 20 degree C for 7 hours under dynamic conditions. The test compound concentration was calculated from the weight difference of the vessels before and after the test and from the air flow through the chamber. he animals were observed for 14 days, after which the survivors were sacrificed. All animals were subjected to gross pathological examination.
Result	:	Concentration Results Time of death (mg/m3) (death/toxic signs/#animals) Male: 179 0 /0 /5 - Female: 214 0 /0 /5 - The exposure was tolerated without toxic signs. Gross pathology showed

no indications of test compound-induced gross organ damage.

Source	:	Bayer Corporation Pittsburgh
Reliability	:	(3) invalid Does not meet importnat criteris of current guidelines

14.01.2008 (21)

5.1.3 ACUTE DERMAL TOXICITY

Type	:	LD50
Value	:	> 5000 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	
Doses	:	5000 mg/kg bw
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The test article doses were individually weighed out on aluminium foil (6.5 x 6.5 cm) and made into a paste using cellulose powder (400 mg cellulose powder/g test article). The aluminium foil was applied to the intact dorsal skin, shorn on the previous day, of groups of five rats per sex and dose. An occlusive dressing was used for fastening to the skin. The exposure period was 24 hours. After removal of the dressings the treated skin areas were cleaned with soap and water. Appearance and behaviour were recorded several times on the day of application, and at least once a day thereafter. The post-treatment observation period was 14 days. Body weights were recorded before application and then on day 4, 8 and 15.

Result : There were no mortalities or clinical signs. The treatment sites of some animals exhibited redness and escharosis from day 2 to day 5 post-treatment. There was no indication of macroscopic damage to organs related to the test article.

Source	:	Bayer Corporation Pittsburgh
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

14.01.2008 (17) (18)

Type	:	LD50
Value	:	> 5000 mg/kg bw
Species	:	rat
Strain	:	Wistar
Sex	:	male/female
Number of animals	:	10
Vehicle	:	other: cellulose powder
Doses	:	5000 mg/kg bw
Method	:	OECD Guide-line 402 "Acute dermal Toxicity"
Year	:	1981
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The dose was weighed individually, made into a paste with cellulose powder, and applied on the unabraded back skin that had been shaved the previous day. 5 rats per sex per dose were tested. The treated areas were covered with aluminum foil and wrapped by bandage. After a 24 hour

exposure period, the bandages and test substance were removed and the skin washed with soap and water.
The animals were observed for 14 days, after which the survivors were sacrificed. All animals were subjected to gross pathological examination.
The median lethal dose (LD50) was calculated by computer (HP 3000) by the method of AP Rosiello, JM Essigmann, and GN Wogan 1977. J. Tox. Environ. Health. 3:797-809).

Result : The treatment was tolerated without clinical signs or mortality. No local findings were observed on the treated area. Gross pathology found no indications of test compound-induced gross damage to visceral organs.
Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
14.01.2008 (21)

5.1.4 ACUTE TOXICITY, OTHER ROUTES

5.2.1 SKIN IRRITATION

Species : rabbit
Concentration : undiluted
Exposure : Semiocclusive
Exposure time : 4 hour(s)
Number of animals : 3
Vehicle :
PDII :
Result : not irritating
Classification : not irritating
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year :
GLP : yes
Test substance : other TS: HWG 1608 alkylketone; active ingredient = 95.4%

Result : Rabbit Irritation Indices

No.	erythema/eschar	edema
1.	0.0	0.0
2.	0.0	0.0
3.	1.3	0.0

Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
14.01.2008 (19)

Species : rabbit
Concentration : undiluted
Exposure : Occlusive
Exposure time : 4 hour(s)
Number of animals : 3
Vehicle :
PDII : 1.8
Result : slightly irritating
Classification : not irritating
Method : OECD Guide-line 404 "Acute Dermal Irritation/Corrosion"
Year : 1981
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Result : Rabbit Irritation Indices

No.	erythema/eschar	edema
1.	1.7	0.0
2.	2.0	0.0
3.	1.7	0.0

Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
14.01.2008 (21)

5.2.2 EYE IRRITATION

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 24 hour(s)
Comment : rinsed after (see exposure time)
Number of animals : 3
Vehicle :
Result : not irritating
Classification : not irritating
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1988
GLP : yes
Test substance : other TS: HWG 1608 alkylketone; active ingredient = 95.4%

Result : All irritation indices (1 hr through 21 days)= 0.0
Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
14.01.2008 (19)

Species : rabbit
Concentration : undiluted
Dose : .1 ml
Exposure time : 24 hour(s)
Comment : rinsed after (see exposure time)
Number of animals : 3
Vehicle :
Result : not irritating
Classification : not irritating
Method : OECD Guide-line 405 "Acute Eye Irritation/Corrosion"
Year : 1981
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Source : Bayer Corporation Pittsburgh
Reliability : (1) valid without restriction
Guideline study
14.01.2008 (21)

5.3 SENSITIZATION

5.4 REPEATED DOSE TOXICITY

Type : Sub-acute
Species : rat

Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	Premating phase: 2 weeks; Mating: 14days; Gestation: ca. 22 days; and Lactation: up to Day 4.
Frequency of treatm.	:	daily
Post exposure period	:	no
Doses	:	0 (vehicle), 15, 80 and 400 mg/kg bw/d
Control group	:	yes, concurrent vehicle
NOAEL	:	80 mg/kg bw
Method	:	other: OECD TG 422
Year	:	2007
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method :

In this study, forty-eight female and forty-eight male Wistar rats were assigned to one of four treatment groups (12 animals/sex/group): 0 (vehicle), 15, 80 and 400 mg Folicur alkylketone/kg body weight/day. Doses were administered by oral gavage in the vehicle (2% Cremophor in deionized water) at a dosage volume of 5 ml/kg. Doses were administered at approximately the same time each day. Dosing volume was adjusted based on the most current body weight during the dosing period. In-life phases included: Premating phase: 2 weeks; Mating: 14 days; Gestation: approximately 22 days; and Lactation: up to Day 4. Body weight and food consumption determinations and detailed clinical examinations of each animal were conducted
weekly throughout the study, as well as, an evaluation of multiple reproductive parameters. Hematology and clinical chemistry was performed for six fasted rats/sex/group and urinalysis was performed on six males/group. Functional Observational Battery and motor activity was also performed on the first six male rats/group and six randomly selected lactating female rats/group. All animals placed on study were subject to a postmortem examination, which included (1) documenting and saving all gross lesions, (2) weighing designated organs and, (3) collecting representative tissue specimens for histopathologic evaluation.

Result :

There were no clinical observations, effects on body weight, motor or non-locomoter effects, effects on organ weights, or microscopic changes in the 15 or 80 mg/kg bw/d groups.

In the 400 mg/kg bw/d groups, clinical observations included urogenital staining and salivation after dosing. A decline in body weight gain was observed in the males with only slight declines in absolute body weight. Motor and locomotor activity was non-statistically decreased when compared to the controls. A slight decline in terminal body weight was observed in the males when compared to controls. Increased liver and kidney weights were observed.
Morphologic changes were characterized as hepatocellular hypertrophy in both sexes and nephropathy (presumptive alpha 2U-globulin) in males.

Test substance	:	99.2% pure
Conclusion	:	The parental systemic LOAEL is 400 mg/kg/day in males and females, based on clinical observations of urogenital staining and salivation, declines in body weight gain and terminal body weight (males only), decreased motor and locomotor activity and increased liver and kidney weights associated with hepatocellular hypertrophy in both genders and nephropathy (presumptive alpha 2U-globulin) in the males. The parental systemic NOAEL is 80 mg/kg bw/day in both genders.
Reliability	:	(1) valid without restriction Guideline study
Flag	:	Critical study for SIDS endpoint

10.01.2008 (11)

5.5 GENETIC TOXICITY 'IN VITRO'

Type	:	Ames test
System of testing	:	Salmonella typhimurium TA 98, TA 100, TA 1535, TA 1537
Test concentration	:	8, 40, 200, 1000, 5000 ug/plate (Ames test); 12.5, 25. 50, 100, 200, 400 ug/plate (preincubation test)
Cycotoxic concentr.	:	> 25 ug/plate
Metabolic activation	:	with and without
Result	:	negative
Method	:	OECD Guide-line 471
Year	:	1994
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : The test followed Ames et al. standard procedure. Four replicates per strain and dose (including the negative and positive control), with and without S9 mix were tested. In the first assay the plate incorporation method was employed. in the second assay the preincubation method was used.

A test is defined as positive if a reproducible and dose-related increase of mutant colonu numbers becomes apparent for at least one strain. For TA 1535, TA 100, and TA 98 mutant colony numbers shoudl increase by a factor of 2 or more over negative control numbers, while at least a three-fold increase shoudl be apparent for TA 1537. Otherwise the result is judged as negative.

Result : Doses up to and including 25 ug/plate did not cause any beacteriotoxic effects: Total bacteria counts remained unchanged and no growth inhibition was observed. The substance revealed weak, strain specific bacteriotoxic effects at higher doses yet doses up to 5000 ug/plate coudl still be used in most cases for assessment purposes. There was no evidence for mutagenic effects of Alkylketon with and without S9 mix. A biologically relevant increase of the mutant count over control levels was not observed. The positive controls revealed marked mutagenic effects as indicated by biologically relevant increase of mutant colony numbers over colony numbers of the negative controls.

Mean revertants/plate without/with S9 (Ames test)

ug/plate	TA1535	TA100	TA1537	TA98
negative				
control	18/17	111/139	14/11	27/38
8	17/18	106/126	11/11	27/40
40	22/18	113/143	12/13	21/39
200	17/14*	94/122	9/12	29/36
1000	7/5*	35/48*	-/-*	18/35
2000	5/3*	28/39*	-/-*	19/32*
Na azide	912/-	-/-	-/-	-/-
2-AA	-/182	-/1780	-/255	-/1674
NF	-/-	408/-	-/-	-/-
4-NPDA	-/-	-/-	106/-	87/-

Mean revertants/plate without/with S9 (preincubation test)

ug/plate	TA1535	TA100	TA1537	TA98
negative				
control	16/17	130/147	9/11	27/40
12.5	20/18	119/146	11/13	28/38
25	20/18	120/143	10/10	31/32
50	20/15	107/129	10/11	20/36
100	18/17*	91/116*	8/10	25/32

200	18/17*	83/98*	7/6	21/29*
400	8/13*	34/73*	5/8*	24/32*
Na azide	878/-	-/-	-/-	-/-
2-AA	-/169	-/1163	-/214	-/1097
NF	-/-	444/-	-/-	-/-
4-NPDA	-/-	-/-	81/-	91/-

* = bacteriotoxic effect

Source : Bayer Corporation Pittsburgh
Test substance : The test substance was shown to be stable in the vehicle at room temperature at concentrations of 0.08 and 50 mg/ml.
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
31.01.2008 (5)

5.6 GENETIC TOXICITY 'IN VIVO'

Type : Micronucleus assay
Species : rat
Sex : male
Strain : other: CD®(SD)IGS BR
Route of admin. : gavage
Exposure period : one treatment
Doses : 0, 500, 100, 2000 mg/kg bw
Result : negative
Method : OECD Guide-line 474 "Genetic Toxicology: Micronucleus Test"
Year : 2007
GLP : yes
Test substance : as prescribed by 1.1 - 1.4

Method : Based on the results of a dose range-finding study, the high dose chosen was 2000 mg/kg, the limit dose based on regulatory guidelines. In the micronucleus assay,
the test article was formulated in 2% Cremophor in deionized water and administered
once by gavage to groups of 5 male rats at 0, 100, 500 and 2000 mg/kg bw. The Positive Control was Cyclophosphamide.
Bone marrow was extracted at 24 hours (5 animals from all groups) and 48 hours (5 aanimals from the control and high dose group) and at least 2000 PCEs per animal were analyzed for the frequency of micronuclei.
Cytotoxicity was assessed by scoring the number of PCEs and normochromatic erythrocytes (NCEs) in at least the first 500 total erythrocytes for each animal.
Result : The test article did not induce signs of clinical toxicity in the animals treated at dose levels up to 2000 mg/kg (the limit dose based on regulatory guidelines). The test article did not induce statistically significant increases in micronucleated PCEs at any test article dose examined (500, 100, and 2000 mg/kg). In addition, the test article was not cytotoxic to the bone marrow (i.e., no statistically significant decreases in the PCE:NCE ratios) at any dose of the test article.
The test article was evaluated as negative in the rat bone marrow micronucleus assay under the conditions of this assay.
Reliability : (1) valid without restriction
Guideline study
Flag : Critical study for SIDS endpoint
11.01.2008 (12)

5.7 CARCINOGENICITY

5.8.1 TOXICITY TO FERTILITY

Type	:	One generation study
Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	Premating phase: 2 weeks; Mating: 14 days; Gestation: ca. 22 days; and Lactation: up to Day 4
Frequency of treatm.	:	daily
Premating exposure period		
Male	:	2 weks
Female	:	2 weeks
Duration of test	:	as above
No. of generation studies	:	1
Doses	:	0 (vehicle), 15, 80 and 400 mg/kg bw/day
Control group	:	yes, concurrent vehicle
NOAEL parental	:	400 mg/kg bw
NOAEL F1 offspring	:	400 mg/kg bw
Result	:	no toxicity to fertility at the highest dose tested
Method	:	OECD Guide-line 422
Year	:	2007
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : In this study, forty-eight female and forty-eight male Wistar rats were assigned to one of four treatment groups (12 animals/sex/group): 0 (vehicle), 15, 80 and 400 mg Folicur alkylketone/kg body weight/day. Doses were administered by oral gavage in the vehicle (2% Cremophor in deionized water) at a dosage volume of 5 ml/kg. Doses were administered at approximately the same time each day. Dosing volume was adjusted based on the most current body weight during the dosing period. In-life phases included: Premating phase: 2 weeks; Mating: 14 days; Gestation: approximately 22 days; and Lactation: up to Day 4. Body weight and food consumption determinations and detailed clinical examinations of each animal were conducted
weekly throughout the study, as well as, an evaluation of multiple reproductive parameters. Hematology and clinical chemistry was performed for six fasted rats/sex/group and urinalysis was performed on six males/group. Functional Observational Battery and motor activity was also performed on the first six male rats/group and six randomly selected lactating female rats/group. All animals placed on study were subject to a postmortem examination, which included (1) documenting and saving all gross lesions, (2) weighing designated organs and, (3) collecting representative tissue specimens for histopathologic evaluation.

Result : There were no test substance-related effects on any reproductive parameter (e.g., mating, fertility, or gestation indices, days to insemination, gestation length, or number of implants) at any dose tested. No test substance-related effects were observed on mean litter size at any dose level.

Test substance : 99.2% pure

Conclusion : The reproductive NOEL is 400 mg/kg bw/day in both males and females based on no
reproductive findings observed in the highest dose tested.

Reliability : (1) valid without restriction
Guideline study

Flag : Critical study for SIDS endpoint
10.01.2008 (11)

5.8.2 DEVELOPMENTAL TOXICITY/TERATOGENICITY

Species	:	rat
Sex	:	male/female
Strain	:	Wistar
Route of admin.	:	gavage
Exposure period	:	Premating phase: 2 weeks; Mating: 14 days; Gestation: ca. 22 days; and Lactation: up to Day 4.
Frequency of treatm.	:	daily
Duration of test	:	see above
Doses	:	0 (vehicle), 15, 80 and 400 mg/kg bw/d
Control group	:	yes, concurrent vehicle
NOAEL maternal tox.	:	80 mg/kg bw
NOAEL teratogen.	:	80 mg/kg bw
other: LOAEL Offspring	:	400 - mg/kg bw
Result	:	No developmental toxicity/teratogenicity at highest dose tested
Method	:	other: OECD TG 422
Year	:	2007
GLP	:	yes
Test substance	:	as prescribed by 1.1 - 1.4

Method : In this study, forty-eight female and forty-eight male Wistar rats were assigned to one of four treatment groups (12 animals/sex/group): 0 (vehicle), 15, 80 and 400 mg Folicur alkylketone/kg body weight/day. Doses were administered by oral gavage in the vehicle (2% Cremophor in deionized water) at a dosage volume of 5 ml/kg. Doses were administered at approximately the same time each day. Dosing volume was adjusted based on the most current body weight during the dosing period. In-life phases included: Premating phase: 2 weeks; Mating: 14 days; Gestation: approximately 22 days; and Lactation: up to Day 4. Body weight and food consumption determinations and detailed clinical examinations of each animal were conducted
weekly throughout the study, as well as, an evaluation of multiple reproductive parameters. Hematology and clinical chemistry was performed for six fasted rats/sex/group and urinalysis was performed on six males/group. Functional Observational Battery and motor activity was also performed on the first six male rats/group and six randomly selected lactating female rats/group. All animals placed on study were subject to a postmortem examination, which included (1) documenting and saving all gross lesions, (2) weighing designated organs and, (3) collecting representative tissue specimens for histopathologic evaluation.

The number of live and stillborn pups were recorded for each litter. Pups were observed daily for clinical signs (cage-side, as described for the adults) from birth until lactation Day 4. In the event a possible clinical sign was observed during the cage-side evaluation, the pup may have been removed from the cage and a more detailed assessment conducted. A detailed clinical observation and a physical examination were performed on each day the pups were weighed. Any abnormal behavior of offspring was recorded. Pups were sexed and their body weights were recorded as soon as possible following parturition (lactation Day 0). Pup weights were also recorded on lactation Day 4.

Result : No test substance-related effects were observed on mean litter size at any dose level. There were no test substance-related clinical observations or effect on the viability of the pups at any dose level tested.Birth weight was not affected by exposure to the test article at any dose level tested. Slight

declines in both male and female pup weight and pup weight gain were observed in the 400
mg/kg/day group. Effects on the pups are considered to be secondary to the toxicity observed in the females at this same dose level.

Test substance : 99.2% pure

Conclusion : The offspring LOAEL is 400 mg/kg bw/day. The LOAEL is based on maternal effects leading to secondarily-mediated effects on pup weight gain. The offspring NOAEL is 80 mg/kg bw/day.

Reliability : (1) valid without restriction
Guideline study

10.01.2008 (11)

5.8.3 TOXICITY TO REPRODUCTION, OTHER STUDIES

5.9 SPECIFIC INVESTIGATIONS

5.10 EXPOSURE EXPERIENCE

5.11 ADDITIONAL REMARKS

6.1 ANALYTICAL METHODS

6.2 DETECTION AND IDENTIFICATION

7.1 FUNCTION

7.2 EFFECTS ON ORGANISMS TO BE CONTROLLED

7.3 ORGANISMS TO BE PROTECTED

7.4 USER

7.5 RESISTANCE

8.1 METHODS HANDLING AND STORING

8.2 FIRE GUIDANCE

8.3 EMERGENCY MEASURES

8.4 POSSIB. OF RENDERING SUBST. HARMLESS

8.5 WASTE MANAGEMENT

8.6 SIDE-EFFECTS DETECTION

8.7 SUBSTANCE REGISTERED AS DANGEROUS FOR GROUND WATER

8.8 REACTIVITY TOWARDS CONTAINER MATERIAL

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(3) Bayer Ag (1993)

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(5) Bayer AG (1994) Salmonella/Microsome Test (plate Incorporation and preincubation method). Study No. T 4049326

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(10) Bayer CropScience (2007) Toxicity of HWG 1608 Alkylketone Technical to the Green Alga Pseudokirchneriella subcapitata. LABORATORY PROJECT ID EBHWY003

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10.1 END POINT SUMMARY

10.2 HAZARD SUMMARY

10.3 RISK ASSESSMENT